REMARKS

Claims 1, 3-5, 7-13, 15, 16, 18-22, 66-85 are pending. Claims 1, 5, 9-12, 20, 22, 66, 68, 69, 70 and 78 have been amended. Support for the claim amendments can be found throughout the application as originally filed.

Applicants thank Examiner Boesen for the telephone interview of April 10, 2008 with the Applicants' attorney, Laurie Butler Lawrence. Various amendments to the claims were discussed which overcome the assertion by the Office that various antibodies needed to be deposited with the ATCC.

If the Examiner determines that there are additional issues not addressed in the last Office Action or this Reply, Applicants' request that the Examiner call the undersigned, Laurie Butler Lawrence, at 617-395-7088 to discuss.

Rejection Under 35 U.S.C. §112, first paragraph

Claims 1, 3-5, 7-13, 15, 16, 18-22 and 66-85 are rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement. The Office alleges that

> It is apparent that antibodies 1D9, HF 21/28 and 4B4'CL are required to practice the claimed invention because they are a necessary limitation for the success of the invention as stated in the claims. The antibodies recited in the claims must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements ... may be satisfied with a deposit.

Applicants respectfully traverse this rejection. The sequences of the variable chains of 1D9, HF 21/28 and 4B4'CL are disclosed in the present application. However, in the interest of expediting prosecution, the claims have been amended to reference the sequences of the variable domains of these antibodies instead of their designated names.

The claims, as amended, recite an isolated nucleic acid molecule encoding a humanized immunoglobulin light chain or antigen-binding fragment thereof and a humanized immunoglobulin heavy chain or antigen binding fragment thereof that bind to CC chemokine receptor 2 (CCR2). The isolated nucleic acid molecule encoding the light chain includes the

three CDRs of the variable light chain of murine antibody 1D9, as shown in SEQ ID NO:9 and a human light chain framework region from the light chain of the human HF 21/28 antibody, as shown in SEQ ID NO:11. The isolated nucleic acid molecule encoding the heavy chain includes the three CDRs of the variable heavy chain of murine antibody 1D9, as shown in SEQ ID NO:10 and a human heavy chain framework region from the heavy chain of the human 4B4'CL antibody, as shown in SEQ ID NO:16. With the guidance provided in the present application, one of ordinary skill in the art at the time of filing could make and use the claimed nucleic acids without undue experimentation.

The application provides a significant amount of information regarding the sequences of murine antibody 1D9, the light chain variable region of the human antibody HF 21/28 and the heavy chain variable region of the human antibody 4B4'CL. For example, as described on page 15, and depicted in Figure 11, the amino acid sequence of the light chain of murine 1D9 is shown. In addition, Figure 11 shows the amino acid sequence of each of the CDRs of the light chain of murine antibody 1D9. Figure 11 also shows the amino acid sequence of the light chain of human antibody HF 21/28 and distinguishes between which portions of the sequence are the framework regions and which are CDRs. Figure 11 also depicts 5 different humanized light chain variable regions that have the three CDRs of murine antibody 1D9 and a framework region of the light chain of human antibody HF21/28. Furthermore, pages 91-95 describe how four of the exemplified humanized light chains were made. With regards to the heavy chain, Figure 12 depicts the amino acid sequence of the heavy chain of murine 1D9. In addition, Figure 12 shows the amino acid sequence of each of the CDRs of the heavy chain of murine antibody 1D9. Figure 12 also shows the amino acid sequence of the heavy chain of human antibody 4B4'CL and distinguishes between which portions of the sequence are the framework regions and which are CDRs. Figure 12 also depicts 4 different humanized heavy chain variable regions that have the three CDRs of murine antibody 1D9 and a framework region of the heavy chain of human antibody 4B4'CL. Furthermore, pages 95-97 describe how the exemplified humanized heavy chains were made. Using this information, a skilled artisan could make and use nucleic acid molecules which encode the humanized light chains and humanized heavy chains recited in the claims. Thus, the claims are enabled and Applicants request that this rejection be withdrawn.

Claims 1, 3-5, 7-13, 15, 16, 18-22 and 66-85 are rejected under 35 U.S.C. §112, first paragraph "because the specification does not reasonably provide enablement for a nucleic acid encoding an antibody without a known binding specificity."

The claims have been amended to recite that the encoded light chains and heavy chains bind to CC chemokine receptor 2 (CCR2), thereby obviating this rejection.

Rejection Under 35 U.S.C. §101

Claims 22 and 66 are rejected under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. Specifically, the Office alleges that the "Claims as written, does not sufficiently distinguish over genes as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products."

Applicants respectfully disagree. Claims 22 and 66 are directed to nucleic acids encoding a *humanized* light chain or heavy chain, thus by definition, these nucleic acids encode something that does not occur in nature. However, to expedite prosecution, claims 22 and 66 have been amended to recite an isolated nucleic acid. Therefore, Applicants respectfully request that this rejection be withdrawn.

Obviousness-Type Double Patenting

Claims 1, 5, 13, 15, 16, 18-22 and 80 are rejected "on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-74 of U.S. Patent No. 6,696,550 ["the '550 patent"]." According to the Office

> Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are drawn to an isolated nucleic acid encoding a humanized immunoglobulin light chain and heavy chain of the murine 1D9 antibody … and the patented claims are drawn to antibodies with binding specificity for CCR2, wherein the antibody binding regions are from the 1D9 antibody and the framework regions are from the HF 21/28 and 4B4'CL antibodies. (emphasis added)

Applicants respectfully traverse this rejection. Applicants note that a restriction requirement was issued in the present application on March 10, 2006 that distinguished nucleic

acids (groups I-III), humanized immunoglobulin light chains (group XI), humanized immunoglobulin heavy chains (group XII), and humanized immunoglobulins or an antigen binding fragments thereof (group XIII). Thus, it is improper to maintain that nucleic acid claims and antibody claims are not patentably distinct when the Office has already alleged that these inventions are distinct. Withdrawl of this rejection is respectfully requested.

Claims 1, 5, 13, 15, 16, 18-22, 66 and 80 are rejected "on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 11-38 of U.S. Patent No. 6,312,689 ["the '689 patent"]."

Applicants respectfully traverse this rejection. The claims of the '689 patent, like the claims of the '550 patent discussed above, are directed to antibodies, whereas the claims of the present application are directed to nucleic acids. As indicated in the restriction requirement issued in the present application, according to the Office, these are distinct inventions. Therefore, Applicants respectfully request that this rejection be withdrawn.

Claims 1, 5, 13, 15, 16, 18-22, 66 and 80 are rejected "on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-51 of U.S. Patent No. 6,727,349 ["the '349 patent"]."

Applicants respectfully traverse this rejection. The claims of the '349 patent, like the claims of the '550 patent discussed above, are directed to antibodies, whereas the claims of the present application are directed to nucleic acids. As indicated in the restriction requirement issued in the present application, according to the Office, these are distinct inventions. Therefore, Applicants respectfully request that this rejection be withdrawn.

An extension fee is being paid concurrently by deposit account authorization. Please charge any deficiency to Deposit Account No. 50/2762, referencing attorney docket number M2051-701840.

Respectfully submitted,

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